

### Just What Is the Li-Fraumeni Syndrome?<sup>1</sup>

The Li-Fraumeni syndrome (LFS) is the familial tendency to develop soft-tissue sarcomas, breast cancers and other neoplasms in children and young adults. This syndrome began with the observation that a child with a rare form of cancer had a father with leukemia and unknown types of cancers in other relatives. Using classic epidemiological detective skills prior to the advent of molecular biology tools available today, Drs. Frederick Li and Joseph Fraumeni in 1969 reported that they were able to identify four different families with these similar cancer tendencies of rare soft-tissue sarcoma, breast cancer and other cancers occurring in younger people. In 1990, using the advances in molecular biology, Li and Fraumeni reported that those with the LFS had a germ line mutation in their p53 tumor suppressor gene. That is, those with Li-Fraumeni syndrome were born with a defect in the gene that prevents the occurrence of cancer, causing them to have cancer at a young age. Thus, the LFS marked the first identification of the common molecular basis for genetic susceptibility to a number of different cancers. For further information, consult the website, <http://www.geneclinics.org/profiles/li-fraumeni/>

<sup>1</sup> Summarized by Kenneth C. Chu, Ph.D., Program Director, Office of Special Populations Research, National Cancer Institute/National Institutes of Health, Bethesda, MD.

Dr. Li's pioneering discoveries and lifelong contributions and achievements in medicine and in cancer prevention and control research specifically has earned him the American Cancer Society's 1999 Medal of Honor in Clinical Research, the highest honor bestowed by the Soci-

ety. Two others who received the American Cancer Society's Medal of Honor in 1999 were Leland Hartwell, Ph.D., President of the world-class Fred Hutchinson Cancer Research Center and C. Everett Koop, M.D., former U.S. Surgeon General.

### Retrospective Views of Frederick P. Li, M.D., M.A.

*Editorial notes: In his brief commentary (page 93), Dr. Frederick Li named two people who contributed to his professional development: Robert W. Miller, M.D. and Joseph F. Fraumeni, Jr., M.D. of the National Cancer Institute (NCI). With the assistance of Kenneth C. Chu, Ph.D. of the NCI, two of Dr. Li's mentors were found and shared these insights about Dr. Li.*

**Robert W. Miller, M.D.**

Scientist Emeritus  
Clinical Genetics Branch  
Division of Cancer Epidemiology  
and Genetics  
National Cancer Institute

Fred's ability to conquer adversity is immense. He came to the Epidemiology Branch of NCI in 1967 and stayed for 24 years. The first test of his ability was in writing up a draft of research results. It was so terrible that I

thought he was too far behind to catch up. He did catch up, very soon, and ever since has been a champion medical writer.

He spoke Cantonese. His intended bride said I cannot marry you until you speak Mandarin. He learned it almost overnight.

His medical training was before the age of molecular biology. He looked for an avenue to take him there and found in it Stephen Friend's nearby laboratory at Harvard. They linked a family cancer syndrome Fred and Joe Fraumeni had identified, to the very important p53 gene, a germ-line mutation which affects

Dr. Li was born in Canton, China and raised in New York City where his parents operated a Chinese restaurant. While growing up, he helped in his parents' restaurant and worked to help his family. He received an A.B. in Physics from New York University, M.D. from University of Rochester, and Master's Degree (Demography) from Georgetown University. In 1967, he joined the Epidemiology Branch, National Cancer Institute, and served for 24 years, mostly at the National Cancer Institute Field Station at the Dana-Farber Cancer Institute in Boston. In 1991, he was appointed the Head of the Division of Cancer Epidemiology and Control at Dana-Farber, and full-time member of the Harvard faculty. Currently, Dr. Li is Professor of Clinical Cancer Epidemiology at Harvard School of Public Health and Professor of Medicine at Harvard Medical School and the Harry and Elsa Jiler American Cancer Society Clinical Research Professor.

Among Dr. Li's numerous honors and distinctions are his winning of the Harvey Cushing Prize in 1965 for "The History of Cholera in

China", the Senior Scholar Award by the Committee on Scholarly Communication with the People's Republic of China by the National Academy of Sciences in 1980, the U.S. Public Health Service Meritorious Service Medal in 1989, the 1989 General Motors Cancer Research Foundation Symposium, and along with Joseph Fraumeni, Jr. received the Charles S. Mott Prize given by the General Motors Cancer Research Foundation in 1995.

Dr. Li has been a member of the Presidentally-appointed National Cancer Advisory Board of National Cancer Institute since 1996. In 1997, he was appointed the Editor-in-Chief of *Cancer Epidemiology Biomarkers & Prevention*. He is the author/co-author of 186 original reports typically published in the most prestigious scientific and medical journals and 71 reviews that have been appeared in reference texts and in publications such as *Scientific American*.

Besides his landmark achievements in clinical cancer research, Dr. Li has never forgotten his Asian American roots. For example, soon

various cellular functions, including the risk of an array of cancers.

It wasn't all luck.

#### **Joseph F. Fraumeni, Jr., M.D.**

Director, Division of Cancer Epidemiology  
and Genetics  
National Cancer Institute

Not long after Fred Li arrived at the National Cancer Institute in the late 1960s as a young research associate, it was clear that he was destined for stardom in medical research. He had an unusually broad awareness of clinical, laboratory, epidemiological and public health issues in oncology, and he was adept in linking different approaches through an innovative interdisciplinary strategy that is now

referred to as "molecular epidemiology". Fred was always open to new ideas and developments from a number of fields, and especially alert to unusual clinical occurrences and epidemiological patterns that provided new leads to cancer etiology. Fred was brilliant in identifying and formulating a key question in cancer etiology, and then efficiently settling the issue by an appropriate study, or by a logical progression of studies as in the case of Li-Fraumeni syndrome.

Another important trait was his friendly and generous nature that fostered the collaborative efforts and teamwork that are often needed in molecular epidemiology. While I may have served as one of Fred's mentors in the early stage of his career, it did not take long for our relationship to evolve into a close and enduring partnership and friendship.